REMARKS

Claims 27-40 are pending in the subject application. By this Amendment, applicants have hereinabove amended claims 27, 28, 33 and 39. In addition, applicants have hereinabove cancelled claim 34 without disclaimer or prejudice to applicants' right to pursue the subject matter of this claim in the future. Support for the amendments to claim 27 can be found in the specification as originally filed at page 16, lines 3 to 13 and line 20; page 83, lines 7 to 16; page 20, lines 12-14; and Fig. 13. Support for the amendments to claim 28 can be found in the specification as originally filed at page 16, line 20; page 16, line 35 to page 17, line 10; page 83, lines 7 to 16; page 20, lines 12-14; and Fig. 13. Support for the amendments to claim 33 can be found in the specification as originally filed at page 19, line 25 to page 20, line 5; page 83, lines 7 to 16; page 20, lines 12-14; and Fig. 13. Support for the amendments to claim 39 can be found in the specification as originally filed at page 22, lines 1-3; page 20, lines 12-14; and page 83, lines 7-16.

After entry of this Amendment, claims 27-33 and 35-40 will be pending and under examination.

Rejection Under 35 U.S.C. §112, First Paragraph (Enablement)

The Examiner rejected claims 28-33, 35-38 and 40 under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification. The Examiner stated that the specification, while

being enabling for an *in vitro* method of increasing a target cell's susceptibility to DNA damaging agents comprising the administration of antisense that inhibit the expression of human Ku70, does not reasonably provide for *in vivo* methods comprising administration by any route or means of antisense to human ku70.

In response, applicants respectfully traverse the Examiner's rejection.

However, in order to expedite prosecution and without conceding the correctness of the Examiner's position, applicants have hereinabove amended claims 28 and 33, from which rejected claims 29-32 and 35-38 depend, to recite that the antisense oligonucleotide having the sequence of a human Ku70 cDNA in the antisense orientation is selectively introduced to the cancer. Applicants maintain that such a method is enabled. In addition, applicants note that previous claim 34, which recited that "the antisense oligonucleotide is introduced selectively at the site of the cancer" was not rejected by the Examiner in the February 7, 2008 Office Action as not enabled. Accordingly, applicants maintain that the invention as claimed in amended claims 28-33 and 35-38 is enabled by the specification, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

With regard to claim 40, applicants note that it is well within the skill of one of ordinary skill in the art to make a pharmaceutical composition comprising the recited expression

vector and a carrier. Applicants note that carriers are described at page 22, lines 8-29, and further note that making pharmaceutical compositions is routine. Applicants also note that at a use is apparently acknowledged as enabled by the Examiner, that is the claimed methods wherein the antisense is to be selectively introduced to the site of the tumor or cancer. Accordingly, applicants maintain that the invention as claimed in claim 40, which depends from amended claim 39, is enabled by the specification, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejections Under 35 U.S.C. §103(a)

The Examiner rejected claims 27, 39 and 40 as allegedly obvious over Reeves et al. (J. Biol. Chem., Vol. 26499):5047-5052, 1989) and Milner et al. (Nature Biotech. 15:537-541, 1997), the combination in view of Takiguchi et al. (Genomics, 35:129-135, 1996) and AuYoung et al. (U.S. Patent No. 5,773,580) insofar as the claims are drawn to compositions and methods for increasing a target cell's sensitivity to DNA damaging agents in vitro comprising the administration of an antisense oligonucleotide in an adenoviral expression vector comprising a heat shock promoter, which antisense specifically hybridizes with a nucleic acid encoding a DNA-dependent protein kinase subunit (Ku70) which antisense inhibits the expression of the target ku70 subunit.

In response, applicants respectfully traverse the Examiner's

rejection.

Applicants note that nowhere in Reeves et al. is an antisense nucleic acid which *has the sequence of a human Ku70 cDNA in the antisense orientation* (as recited in rejected claims 27 and 39, from which rejected claim 40 depends) taught or suggested. The remaining cited references in combination with Reeves et al. do not cure this deficiency. With regard to the Examiner's statement that Reed et al. "teach full length antisense sequence to BCL-2", applicants note that this is not predictive of an antisense nucleic acid having the sequence of a *human Ku70 cDNA* in the antisense orientation. Regarding predictability of antisense, Agrawal et al. (Mol. Med. Today, 6:72-81) which was previously cited by the Examiner, state at page 80 that one should "study each … oligonucleotide in its own context, and relevant cell line, without generalizing the results for every oligonucleotide." Accordingly, applicants maintain that the invention as claimed is not obvious over Reeves et al. in combination with the remaining cited prior art, and respectfully request reconsideration and withdrawal of this ground of rejection.

Applicants further note that Milner et al., as cited by the Examiner, discusses that the efficacy of an antisense must be tested, thus indicating that the efficacy of any one antisense molecule is not predictable. Milner states that "surprisingly few [tested] oligonucleotides gave significant heteroduplex yield", (see Abstract). Furthermore, Milner et al. discuss the "variable success that is commonly experienced in the choice of

antisense oligonucleotides", (see Abstract). Applicants maintain that the antisense nucleic acid as recited in claim 39 and 40 is not obvious as its efficacy was not predictable in light of the cited prior art. However, applicants have shown it to work as an antisense (see page 83, lines 7 to 16). In addition, the method of claim 27, which recites the antisense nucleic acid, is not obvious as the efficacy of the particular antisense nucleic acid was not predictable in light of the cited prior art. Accordingly, applicants maintain that the invention as claimed is not obvious over the cited prior art and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Provisional Obviousness-Type Double Patenting Rejection

In the February 7, 2008 Office Action, the Examiner provisionally rejected claims 27, 39 and 40 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1, 15, 16 and 18-22 of copending U.S. Application No. 09/750,410.

Applicants understand that this is only a provisional rejection, and will consider filing a Terminal Disclaimer if necessary should the rejection become non-provisional.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed total fee of $120.00 for a one-month extension of time, is deemed necessary in connection with the filing of this Amendment and Supplemental Information Disclosure Statement. However, if any additional fee is required, authorization is given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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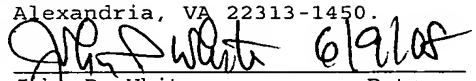

John P. White Date
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